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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/528,172	03/17/2005	Sung Ho Ryu	1751-377	6475

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EXAMINER	
SAIDHA, TEKCHAND	

ART UNIT	PAPER NUMBER
1652	

NOTIFICATION DATE	DELIVERY MODE
03/06/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PTO-PAT-Email@rfem.com

Office Action Summary	Application No.	Applicant(s)	
	10/528,172	RYU ET AL.	
	Examiner	Art Unit	
	Tekchand Saidha	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 January 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) *6-12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

FINAL REJECTION

1. Amendment to claims and arguments filed 1/08/2008 in response to Office Action mailed 8/8/2007 is acknowledged.

2. Claims 1-5 are under consideration in this Office Action.

3. **Claims withdrawn**:

Claims 6-13 remain withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

4. Applicant's arguments filed with the amendment cited above, have been fully considered but they are not deemed to be persuasive. The reasons are discussed following the rejection(s).

5. Any objection or rejection of record not expressly repeated in this Office Action has been overcome by Applicant's response and withdrawn.

6. Claim Rejections - 35 USC § 112 (first paragraph)

Written Description

Claims 1-5 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. These claims are directed to a genus of peptide complexes comprising any phospholipase D (PLD) and actin from any mammalian source and including variants, fragments and fusion peptides comprising PLD and actin from any source with no defined structure or any assigned function to the variant complex. The word peptide being treated as a fragment of the polypeptide of phospholipase or action.

The specification does not contain any disclosure or description of the structure and function of all variant complex sequences having a defined function or activity. Further, the specification as filed does not describe specific assays to measure the various polypeptide complexes having the 'PLD-Actin activity' or which is so evident, as none is described. It is also not known what the function of the claimed complexes are? The genus of peptide complexes that comprise these PLD-actin molecules is a large variable genus with the potentiality of comprising different protein PLD-Actin complexes from a variety of phospholipases and actins

which may or may not have the desired function. Therefore, many functionally unrelated peptide complexes are encompassed within the scope of these claims.

The specification discloses the PLD-2-binding protein from rat brain obtained using the antibody to the rat PLD-2 (of sequence of SEQ ID No. 8) and the identification of rat brain β-actin (43-kDa protein), detected as a PLD2-binding protein of the claimed genus which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. [Other sequences of SEQ ID NO: 9-15 are disclosed but these sequences are structurally distinct and may or may not detect PLD2-binding protein or activity]. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Applicants' arguments:

Citing various articles Applicants respectfully submit that the disclosure of the specification relating to a peptide complex containing rat PLD and rat actin is sufficient to represent the claimed mammal PLDs and mammal actins. As shown in the attached publications, M.A. Frohman et al., Mammalian phospholipase D structure and regulation, Biochimica et Biophysica Acta, 1439, pp 175-186 (1999) ("Frohman") and J.H. Exton, Minireview: Regulation of phospholipase D, FEBS Letters, 531, pp. 58-61 (2002) ("Exton"), various mammalian PLDs were identified and sequenced before the effective filing date of this application. More importantly, the regions having catalytic function are conserved through different species. See page 176 of Frohman and page 58 of Exton.

Similarly, actins from different species exhibit the high sequence conservation among different species. See E.S. Hennessey et al. Review Article: Molecular genetics of actin function, Biochem J., 282, pp 657-671 (1993) ("Hennessey"). With respect to mammalian actins, Hennessey teaches that "[s]keletal muscle mactins in human, mouse, rat, rabbit and chicken are identical, as are the cytoplasmic 13-actins in human, mouse, rat, cow and chicken." See page 657, right column.

Applicants arguments are considered but not found to be persuasive because (1) no copies of the cited references are attached. (2) Further, there is not description presented in the specification regarding the function of the complex so formed. Assuming that the claims as amended now recite 'an isolated peptide complex comprising a 'mammalian phospholipase D' and a 'mammalian actin' as a second peptide, and wherein the prior art teaches a variety of

mammalian PLD and actin, there is no reason to include the structure into the claims because of the well know structures of the mammalian polypeptides in the prior art. However, there is no evidence presented in the instant application that the formation of the 2 peptides into a complex still retains the function one or either of the two polypeptides. This is also not evident from the language of the present claims. The rejection is therefore maintained.

7. ***Enablement Rejection***

Claims 1-5 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a PLD-2-binding protein from rat brain obtained using the antibody to the rat PLD-2 (of sequence of SEQ ID No. 8) and the identification of rat brain β-actin (43-kDa protein), does not reasonably provide enablement for any peptide complex(es) comprising any phospholipase D (PLD) and actin from any source and including variants, fragments and fusion peptides comprising PLD and actin from any source with no defined structure or any assigned function to the variant complex. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The scope of the claims does not commensurate with the enablement provided by the disclosure with regard to the extremely large number of peptide complexes broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the detection of rat PLD2-binding protein using rat PLD2 antibody.

While recombinant and mutagenesis techniques are known, it is <u>not</u> routine in the art to screen for multiple mammalian peptide isolation and the forming of complexes in order to produce PLD-binding protein complexes comprising PLD and actin from any mammalian source or fragments thereof [The word peptide being treated as a fragment of the polypeptide of phospholipase or action], as encompassed by the instant claims, and such

fragments within a protein's sequence which may be combined to form complexes with a reasonable expectation of success having the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of exact nature of the peptide complexes is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Applicants argue that the amended claim 1 specifies a source of the first and second peptides as mammals. Their sequences and the regions that maintain their functions among various mammals are highly conserved. The regions of PLDs or actins responsible for catalytic function are also known.

Thus, one skilled in the art would readily conduct modification of PLDS or actins without affecting their activities. Given the well known knowledge and information available in the relevant field, one skilled in the art would have been able to practice the claimed invention without undue experimentation.

Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection.

As explained in paragraph 6 above, there is no evidence presented in the instant application that the formation of the 2 peptides into a complex still retains the function one or the other of the two polypeptides. This is also not evident from the language of the present claims. The rejection is therefore maintained.

8. Claims 1-5 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific or substantial asserted utility or **a well established utility**.

Applicants disclose a polypeptide complex between rat-PLD2-antibody and rat β-actin. While the rat-PLD2-antibody is useful in detection of rat β-actin (see example 1), no utility is assigned or is apparent to the complex formed between rat-PLD2-antibody and rat

β-actin and therefore the 'isolated peptide complex' comprising a first peptide –PLD, and a second peptide-actin – lack utility.

The specification does not disclose a specific function of the polypeptide complex, its relationship to any disease, or any specific real world use. The specification describes no generic functions for the peptide complex.

It appears that the main utility of the peptide-complex is to carry out further research to identify the biological function and possible diseases associated with said function. Substantial utility defines a real world use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a real world context of use are not substantial utility. Thus, the claimed invention has no specific or substantial asserted utility. Claims 1-5 are also rejected for lack of enablement, since claimed sequences were found to lack utility, since enablement requirement of 35 U.S.C. §112 incorporates utility requirement of 35 U.S.C. §101, and since application that fails as matter of fact to satisfy Section 101 also fails as matter of law to enable person of ordinary skill in art to use invention, as required by Section 112.

Applicants' arguments:

Applicants argue that the specification of this application states that, the claimed complex would be useful for screening a modulator of an interaction between PLD and a PLD binding partner. The modulator, according to the specification, is useful in treating diseases and disorders such as neurodegenerative diseases, autoimmune diseases, cancer and diabetes. See page 2 at paragraphs 5, 6, 56-68. For example, PLDs are overly expressed in certain cancers and actins inhibit the activity of PLDS. See e.g.-. D-Y. Noh et al., Over expression of phospholipase D1 in human breast cancer tissues, Cancer Letters, 161, pp 207-214 (2000). The claimed complex can be used to screen such a modulator that can control the interaction between PLD and actin or stabilizing the peptide complex. Then, the modulator can be used for treating certain cancers in which PLDs are overly expressed, such as breast cancer.

Applicants arguments are considered but not found to be persuasive because the individual use of the polypeptides do not support the use the complex polypeptide, as no evidence exist that the complex is active. Further, page 2 (lines 28-32) of the instant specification states- "For example, a modulator of the peptide complex, including agonist

and antagonist, would be useful in treating diseases and disorders such as neurodegenerative diseases, autoimmune diseases, cancer and diabetes is not considered a specific or substantial asserted utility or a well established utility. The rejection is therefore maintained.

9. No claim is allowed.

10. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tekchand Saidha whose telephone number is (571) 272 0940. The examiner can normally be reached on 8.30 am - 5.00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (571) 272 0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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